

Successful Intravascular Ultrasound Thrombolysis of Dural Sinus Thrombosis with Pre-Existing Subarachnoid and Intraparenchymal Hemorrhages

M.E. ATHERTON, W.C. CULP, A.T. BROWN, E. ERDEM

Department of Radiology, University of Arkansas for Medical Sciences; Little Rock, Arkansas, USA

Key words: thrombolysis, ultrasonography, cerebral veins, cranial sinus

Summary

A case of cerebral venous thrombosis with intraparenchymal and subarachnoid hemorrhages was initially treated unsuccessfully with mechanical and pharmacologic thrombolysis using intrathrombus tissue plasminogen activator (tPA) and angioplasty, and later successfully treated with an intravascular ultrasound tPA infusion catheter. This new microcatheter allowed direct infusion of tPA while using local therapeutic intravascular ultrasound to increase the thrombolytic effect. Flow was quickly restored. Our patient recovered from coma to discharge home without worsening of existing hemorrhages.

Introduction

Thrombosis of dural venous sinuses represents less than 1% of strokes¹. The time-to-presentation, clinical signs and symptoms, imaging findings and outcomes are widely variable making diagnosis and treatment difficult. Heparinization is the usual treatment while focal catheter directed thrombolysis is reserved for worsening patients. Augmentation of pharmacologic thrombolysis with balloon angioplasty and rheolytic catheter thrombectomy have been reported². We report a case of cerebral venous thrombosis (CVT) with intracranial hemorrhage treated with mechanical and pharmacologic thrombolysis using intrathrom-

bus tissue plasminogen activator (tPA), balloon angioplasty, and an intravascular therapeutic ultrasound infusion catheter (EKOS MicroLySUs, EKOS Corporation; Bothell, WA, USA).

Case Report

A 41-year-old man presented to an outside hospital with a five day history of nausea and headache and two days of worsening vomiting, blurry vision, left-sided dysesthesia, and weakness. He was diagnosed with CVT and transferred to our institution. On admission, computed tomography (CT) and magnetic resonance (MR) showed diffuse subarachnoid hemorrhage and focal right basal ganglia hemorrhage with thrombosis of the superior sagittal, bilateral transverse, and left sigmoid sinuses (Figure 1).

On admission the patient was awake but lethargic, oriented with intact speech, demonstrating left-sided neglect with weakness, and intact cranial nerves. A ventricular drain was placed to control elevated intracranial pressure. Due to the placement of the external ventricular drain, there was a delay in starting intravenous heparin. On hospital day two in the neuro-intensive care unit, the patient's condition deteriorated. He was intubated and started on heparin. The following day, mechanical and chemical thrombolysis using a 5mm balloon and 5 mg of intrathrombus tPA resulted in a

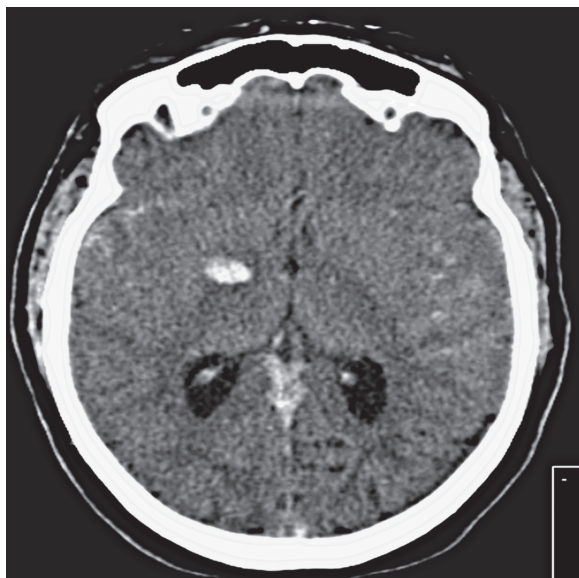


Figure 1 Preliminary CT. Non-contrast head CT prior to catheter directed treatment showing right basal ganglia hemorrhage, subarachnoid hemorrhage, and venous sinus thrombosis.

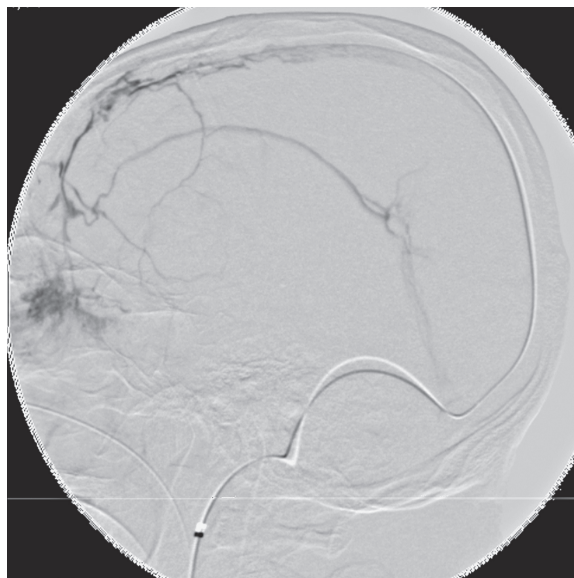


Figure 2 Cerebral venogram. Lateral view with injection through a micro catheter showing near complete occlusion of the superior sagittal sinus and diverted venous flow anteriorly through the inferior sagittal sinus, prior to ultrasound therapy..

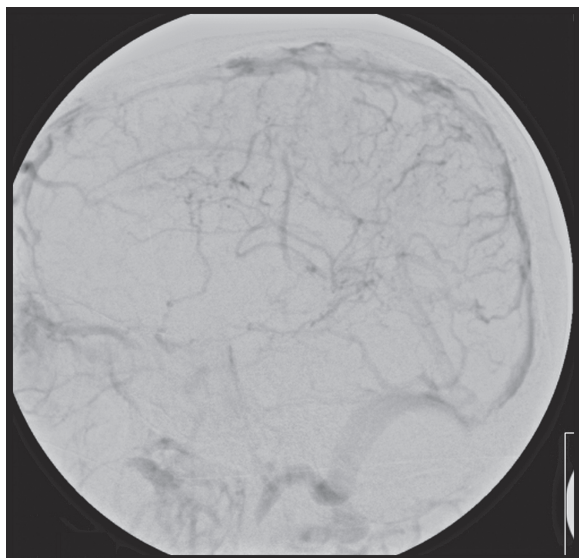


Figure 3 Cerebral angiogram. Venous phase of cerebral angiogram showing improved flow through dural venous sinuses following ultrasound thrombolysis.

small improvement in flow. Over the next two days, he became comatose and continued to deteriorate with increasing intracranial pressure despite drainage and medical management. He returned to interventional radiology for ultrasound augmented thrombolysis (Figure 2).

The 2.5 Fr EKOS MicroLysUS catheter has a 2 mm 2.1MHz ring sonography transducer at its tip (Avg power 0.21-0.45 W) and is FDA approved for injection of contrast into the neurovasculature of humans³.

The microcatheter was positioned within the sagittal sinus thrombus and the clot was laced with 7.5 mg of tPA. While the ultrasound was running, the catheter was slowly withdrawn throughout the length of the clot within the sagittal sinus, torcula, and right transverse sinus over approximately thirty minutes. Flow was immediately restored from total occlusion to near complete recanalization. A stenosis within the right transverse sinus was dilated using a 6 mm balloon. Final internal carotid angiograms

showed greatly improved flow throughout the venous system (Figure 3).

The next 24 hours brought a dramatic improvement in mental status. The coma resolved and he began to follow commands. His intracranial pressures improved. Over the next few days he was weaned from the ventricular drain and ventilator. The amount of sinus thrombosis was markedly decreased without any sign of worsening hemorrhage on repeat CT scans. At discharge home he was awake, alert, oriented, with intact speech and 4/5 left-sided weakness. He was seen in clinic six months later and MRV showed complete recanalization of the cerebral venous system.

Discussion

The diagnosis of CVT can be difficult and is often delayed by the nonspecific nature of the symptoms. Patients often initially experience headaches, nausea and vomiting. These symptoms are thought to be related to increased venous pressure. The symptoms usually progress over sub sequential days to include focal neurological deficits, seizures and decreased mentation⁴.

Traditional treatment for CVT is supportive using hydration, intravenous anticoagulation, intracranial pressure control and treatment of the underlying cause. More aggressive methods have been described including intravenous tPA, mechanical (balloon) thrombolysis, rheolytic thrombolysis, and craniectomy. No single technique has become the dominant therapeutic choice. Given the diversity of patient presentations and outcomes with CVT, it is difficult to imagine a controlled trial evaluating treatments of such a rare form of stroke.

The International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) study group published their multinational prospective observational data on 624 patients with CVT. Only 2.1% of patients were treated with catheter directed thrombolysis⁵. They reported a 30-day case fatality of 3.4% and an overall death or dependency rate of 13%. Coma, cerebral hemorrhage, and malignancy were identified as prognostic indicators of death or dependence. Increased risk of death or dependence was seen in male patients, patients over 37 years, patients with mental status disorder, thrombosis of the deep cerebral system, and central nervous system infection⁵. Our patient

had many of these poor prognostic and risk factors supporting more aggressive treatment.

Thrombus dynamics are multi-factorial and range from prompt autolysis to longstanding resistant thrombus that propagates in the absence of flow. In general, the effective delivery of lytic agent into the clot determines the rate of thrombolysis. In vitro and animal research has shown that ultrasound augments clot lysis by increasing drug transport, reversibly changing the fibrin structure, and increasing tPA binding affinity^{6,7}. Ultrasound reversibly changes the protein structure of the fibrin within the clot which opens more binding sites for fibrinolytic enzymes⁷. It also changes the binding kinetics of tPA to fibrin increasing the rate of clot dissolution⁷.

Enhanced thrombolysis with ultrasound has been demonstrated in human trials. The CLOT-BUST trial randomized 126 patients with middle cerebral artery thrombosis to receive intravenous tPA or intravenous tPA plus transcranial Doppler ultrasound, and showed an increased rate of recanalization in the ultrasound augmented group⁶. The Interventional Management of Stroke (IMS) II trial included patients treated with intra-arterial tPA and intra-arterial localized ultrasound delivery⁸. It showed a trend toward improved revascularization using the intra-arterial ultrasound catheter compared to intra-arterial tPA alone. However, it also showed an increased number of symptomatic intracranial hemorrhages in the ultrasound catheter group⁸.

The risk of increased hemorrhage by using ultrasound was carefully weighed in this patient with existing subarachnoid and basal ganglia hemorrhage. Given his poor neurologic status and the minimal improvement from our previous attempt with tPA and angioplasty, we felt intravascular ultrasound augmentation was warranted. The EKOS catheter provides a 360° pulse wave around the distal tip with an effective range of only a few mm. Here it produced prompt recanalization with excellent flow and no hemorrhagic side effects. The nearby sites of previous hemorrhage showed no sign of increasing bleeding or other complication. The angiographic and clinical outcomes were dramatic without worsening of the existing hemorrhage. However, when considering the success of the EKOS catheter, considerations of its challenges must also be understood. The distal tip of EKOS catheter which contains the US transducer is non-flexible. This can present a

challenge when using the catheter. We have previously ruined an EKOS catheter trying to place it through a 5F nonguide catheter. In this case, placing a 6F guide catheter in the right internal jugular worked well and allowed adequate space for the EKOS.

Data regarding ultrasound augmentation of thrombolysis in central venous thrombosis is limited. It was useful in this patient who was resistant to conventional therapy and had several poor prognostic indicators. Here ultrasound augmented thrombolysis lead to a dramatic improvement and was likely a life saving

treatment. It deserves consideration in patients who do not respond to conventional therapy or have a high likelihood of poor outcome. It appears to be a needed and safe addition to therapeutic options, especially in difficult patients at additional risk of hemorrhage.

Acknowledgement

This work was supported in part by a grant from the National Institutes of Health, NIH R01HL82481.

References

- 1 Hocker SE, Rima DM, Lotfi Hacin-Bey. Successful delayed thrombolysis for cerebral venous and dural sinus thrombosis: A case report and review of the literature. *J Stroke Cerebrovasc Dis.* 2008; 17 (6): 429-432.
- 2 Curtin KR, Shaibani A, Resnick SA, et al. Rheolytic catheter thrombectomy, balloon angioplasty, and direct recombinant tissue plasminogen activator thrombolysis of dural sinus thrombosis with preexisting hemorrhagic infarctions. *Am J Neuroradiol.* 2004; 25: 1807-1811.
- 3 Mahon BR, Nesbit GM, Barnwell SL, et al. North American clinical experience with the EKOS MicroLy-SUS infusion catheter for the treatment of embolic stroke. *Am J Neuroradiol.* 2003; 24: 534-538.
- 4 Lee SK, ter Brugge K. Clinical presentation, imaging and treatment of cerebral venous thrombosis (CVT). *Interventional Neuroradiology* 2002; 8: 5-14.
- 5 Ferro J, Canhao P, Stam J, et al. Prognosis of cerebral vein and dural sinus thrombosis: Results of the international study on cerebral vein and dural sinus thrombosis (ISCVT). *Stroke.* 2004; 35: 664-670.
- 6 Alexandrov A, Molina C, Grotta J, et al. CLOTBUST Investigators. Ultrasound-enhanced systemic thrombolysis for acute ischemic stroke. *N Engl J Med.* 2004; 351: 2170-2178.
- 7 Francis C. Ultrasound-enhanced thrombolysis. *Echocardiography.* 2001; 18: 239-246.
- 8 Tomsick T, Broderick J, Carrozella J, et al. Interventional Management of Stroke II Investigators. Revascularization results in the interventional management of stroke II trial. *Am J Neuroradiol.* 2008; 29: 582-587.

William C. Culp, MD
Department of Radiology
University of Arkansas for Medical Sciences
Slot 556
4301 W. Markham
Little Rock, AR 72205
Tel.: 501-686-6901
Fax: 501-686-6900
E-mail: culpwilliamc@uams.edu